UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/297,701	05/05/99	DEBOUCK	C P505/2

EXAMINER	
SOUAYA, J	
ART UNIT	**PAPER NUMBER**
1655	

DATE MAILED: 10/03/01

020462
SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW22
P. O. BOX 1539
KING OF PRUSSIA PA 19406-0939

HM22/1003

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/297,701	Debrouck et al
Examiner	**Art Unit**
Jehanne Souaya	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 11, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-12* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other: .

DETAILED ACTION

1. Currently, claims 1-12 are pending in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

3. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Nishi et al (JBC, March 1994, vol. 269, pp 6320-6324) and Quandt et al (Gene, 1993, vol. 127, pp 15-21) in view of Lennon et al (Trends in Genetics, October 1991, vol. 7, pp 314-317).

Nishi et al teaches an agent (LMB) that induces arrest of the eukaryotic cell cycle (abstract, fist para of p. 6320). Nishi teaches screening genomic library of LMB-resistant mutants to identify the target gene of LMB (abstract, p. 6320, last para). Nishi teaches comparison of allelic mutation and wild-type (p. 6322, col. 2, fist full para). Nishi teaches the gene and protein sequence of the LMB resistant gene (p. 6322, Table II). Nishi teaches compositions of the agent

LMB (figure 1). Although Nishi does not teach such a method in detecting genes essential to the growth of a single celled organism, one of ordinary skill in the art would recognize that such a method could be used to screen for essential genes in microorganisms. One of ordinary skill in the art would be motivated to screen for essential genes in single celled organisms for the purposes of screening for possible inhibitors of pathogens. Although Nishi does not teach the use of suicide vectors in mutagenizing, Quandt teaches the construction of a set of vector plasmids which greatly facilitate gene replacement and reverse genetics in many Gram-negative bacteria (see abstract). Quandt teaches that these vectors, termed suicide vectors, were used to carry out gene replacement experiments in the fixN region of Rhizobium leguminosarum (see abstract). Quandt teaches using these vectors in the genetic analysis of a wide range of gram negative bacteria and further teach that these vectors offer a number of improvements on existing sacB-based systems which include the ease of cloning fragments into these vectors and the fact that they are mobilisable (see p. 19, col 2 "conclusion"). Quandt teaches that these vectors are extremely useful in eliminating long and tedious screening procedures (see abstract). Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the suicide vectors for the purpose of mutagenizing in the modified method of Nishi as Quandt teaches that these vectors are extremely useful in eliminating long and tedious screening procedures.

Although Nishi does not teach the use of arrayed immobilized library to perform the screening of mutants, Lennon et al teach method of screening libraries involving generating a

plurality of filters that form a grid, each grid containing at a predefined region, immobilized cDNA clones (page 314, col. 2, first para, page 315, col. 1 last para, and col. 2). Lennon also teaches the use of a "genomic" cDNA library (p. 314, col. 2, last para). Lennon teaches screening the filters with a labeled hybridization probe to, for example, identify cDNAs (equivalent to mRNAs) that are differentially expressed between tissues and/or developmental stages or directly comparing two sets of conditions (Table 1, page 316, col. 2, first full para). Lennon teaches that the use of arrayed libraries can be used to eliminate the need for multiple rounds of clone purification, thereby improving screening methods (p 315, col. 2, last para).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the hybridization based screening method of Lennon to have screened for LMB mutations in a population as taught by Nishi to have obtained the invention as a whole. One of ordinary skill in the art at the time of the invention would have been motivated to have used the methods of Lennon for screening to have screened for LMB target genes as taught by Nishi because Lennon teaches that the use of arrayed libraries can be used to eliminate the need for multiple rounds of clone purification, thereby improving screening methods. Thus addition of the method of screening of Lennon to perform the method of Nishi would have made the screening method of Nishi easier to perform.

Response to Arguments

4. The response traverses that the skilled artisan would nut use the method of Nishi and Quandt in view of Lennon to arrive at Applicant's claimed gridding method because if genomic

Dna is extracted from the wild-type LMB sensitive strain and mutant LMB resistant strain and wild-type S. Pombe genomic DNA is used as template for two separate hybridization probes, the genomic grids would not be usable to distinguish between the dominant LMB resistant form of the *crm*1 gene and the recessive *crm1* gene because hybridization patterns due to slight mutations in the essential gene sequences would likely not interfere with DNA-DNA hybridizations and that in fact the whole genome will likely hybridize to the grid forming no patterns in either case. The response further asserts that the cited reference to not teach or suggest using extracted DNA of the test cultures as templates in primer extension reactions where the oligonucleotide primers are directed against the inserted elements and the reaction extends into flanking DNA sequence. This argument has been thoroughly reviewed but was found unpersuasive because the step of generating polynucleotide probes from isolated DNA of the test culture using primers directed against the inserted elements would be considered routine optimization on the part of the ordinary artisan. It was readily known in the art at the time of the invention that false hybridization results could be achieved in hybridization methods depending on the length of the probe (that is it was known that the longest stretch of complementary nucleic acids would likely result in hybridization of two sequences that were not exactly complementary) and the hybridization conditions. The skilled artisan would have known that using genomic DNA to probe would likely have resulted in non-specific hybridization. It would have therefore been prima facie obvious to the ordinary artisan to have generated shorter probes that contained the inserted elements to detect hybridization differences between mutant and wild type strains.

The response further traverses that Lennon does not teach genomic DNA perse and that therefore, Lennon's screen along with the teachings of Nishi and Quandt are not obvious as Lennon's method require the isolation of expressed RNA to produce cDNA. This argument has been thoroughly reviewed but was found unpersuasive. Firstly, the teachings of Lennon were cited to show the general state of the art at the time of the invention. The teachings of Lennon as to a "genomic" cDNA library as a library containing cDNA made from poly(A)+ and poly (A)- RNAs is a characteristic of Lennon's specific method. However, the teaching of Lennon provides the ordinary artisan with teachings that can be more generally applied. Specifically, the teachings of Lennon make it clear that at the time of the invention the art taught screening libraries involving generating a plurality of filters that form a grid, each grid containing at a predefined region, immobilized DNA (page 314, col. 2, first para, page 315, col. 1 last para, and col. 2). Lennon teaches screening the filters with a labeled hybridization probe to identify DNA that is differentially expressed between tissues and/or developmental stages or directly comparing two sets of conditions (Table 1, page 316, col. 2, first full para). Lennon teaches that the use of arrayed libraries can be used to eliminate the need for multiple rounds of clone purification, thereby improving screening methods (p 315, col. 2, last para). Secondly, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. a grid representing a genomic library,) are not recited in the rejected claim(s). Specifically, the claims, at step b of claim 1, are drawn to "(b)providing a plurality of identical grids, each grid comprising a surface on which is immobilized

at predefined regions on said surface a plurality of defined materials *derived* from the genomic library;". The claims do not make clear what is considered "derived from a genomic library", Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. *In re Van Guens*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

5. No claims are allowable.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
September 27, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600
10/1/01